



SEQUENCE LISTING

546
P2
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Radhakrishnan, Balasingam
Price, Christopher
Anderson, Wesley
Ansari, Aslam~~

<120> METHODS FOR INDUCING ANALGESIA

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<141> 1999-10-29

<150> 09/134,803

<151> 1998-08-14

<160> 52

<170> PatentIn version 3.0

<210> 1

<211> 6

<212> PRT

<213> synthetic construct

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<221> MOD_RES

<222> (6)..(6)

<223> Polymer connected to epsilon-amino group

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Tyr Gly Gly Phe Met Lys
1 5

<210> 2

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<223> Polymer connected to alpha-amino group

<220>

<221> MOD_RES

<222> (6)..(6)

<223> Polymer connected to epsilon-amino group

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Tyr Gly Gly Phe Met Lys
1 5

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<222> (1)..(1)
<223> Polymer connected to alpha-amino group

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Tyr Gly Gly Phe Met Lys
1 5

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<223> ACETYLATION

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<222> (6)..(6)
<223> AMIDATION

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Phe Arg Trp Trp Tyr Lys
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<222> (6)..(6)
<223> AMIDATION

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Arg Trp Ile Gly Trp Lys
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<211> 6

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<223> AMIDATION

<220>
<221> UNSURE
<222> (6)..(6)
<223> Xaa can be any of the twenty naturally occurring amino acids

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Trp Trp Pro Lys His Xaa
1          5

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<213> synthetic construct

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<222> (4)..(4)
<223> AMIDATION

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<221> UNSURE
<222> (4)..(4)
<223> Xaa is either Lys or Arg

<400> 7

Trp Trp Pro Xaa
1

<210> 8
<211> 6
<212> PRT
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<221> MOD_RES
<222> (6)..(6)
<223> AMIDATION

<220>
<221> UNSURE
<222> (6)..(6)
<223> Xaa can be any one of the naturally occurring amino acids

<400> 8
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Tyr Pro Phe Gly Phe Xaa
1 5

<210> 9
<211> 7
<212> PRT
<213> synthetic construct

<220>
<221> MOD_RES
<222> (1)..(5)
<223> Amino acids are in the D-form

<220>
<221> MOD_RES
<222> (6)..(6)
<223> n is 0 or 1

<220>
<221> MOD_RES
<222> (7)..(7)
<223> Xaa is Gly or the D-form of a naturally occurring amino acid

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 9

Ile Met Ser Trp Trp Gly Xaa
1 5

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<212> PRT
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<221> MOD_RES
<222> (1)..(4)
<223> Amino acids are in the D-form

<220>
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<222> (6)..(6)
<223> Xaa is Gly or the D-form of a naturally-occurring amino acid

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<223> AMIDATION

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Ile Met Thr Trp Gly Xaa
1 5

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<220>
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<222> (2)..(2)
<223> Xaa is A1, wherein A1 is the D-form of Nve or Nle

<220>
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<222> (3)..(3)
<223> Xaa is B2, wherein B2 is Gly, Phe, or Trp

<220>
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<222> (4)..(4)
<223> Xaa is C3, wherein C3 is Trp or Nap

<220>
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<222> (4)..(4)
<223> AMIDATION

<400> 11

Tyr Xaa Xaa Xaa
1

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<212> PRT
<213> synthetic construct

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<222> (1)..(1)
<223> Tyr has at its N-terminus an Me-x-H-y-N group, wherein x is 0, 1, or 2; and y is 0, 1, or 2, with the proviso that x and y is never greater than

<220>
<221> MOD_RES
<222> (1)..(2)
<223> The amine between the first Tyr and the second Tyr is methylated

<220>
<221> MOD_RES
<222> (3)..(3)

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<223> Xaa is Xaa-z, wherein Xaa is Phe, (D)Phe, or NHBzl, and wherein z  
is 0 or  
  
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<222> (3)..(3)  
<223> AMIDATION  
  
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Tyr Tyr Xaa  
1  
  
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<213> synthetic construct  
  
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<222> (4)..(4)  
<223> Xaa is D4, wherein D4 is Lys or Arg  
  
<220>  
<221> MOD_RES  
<222> (5)..(5)  
<223> His is His-z, wherein z is 0 or 1  
  
<220>  
<221> MOD_RES  
<222> (6)..(6)  
<223> Xaa is Xaa-z, wherein Xaa is a naturally occurring amino acid and  
z is 0 or  
  
<220>  
<221> MOD_RES  
<222> (6)..(6)  
<223> AMIDATION  
  
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Trp Trp Pro Xaa His Xaa  
1 5  
  
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<213> synthetic construct  
  
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<222> (2)..(2)  
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid
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Tyr Xaa Phe Phe
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<211> 4
<212> PRT
<213> synthetic construct

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<222> (4)..(4)
<223> AMIDATION

<400> 15

Tyr Xaa Phe Phe
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<212> PRT
<213> synthetic construct

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<221> MOD_RES
<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Me), i.e. N-alpha-methyltyrosine

<220>
<221> MOD_RES
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 16

Tyr Xaa Phe Phe
1

<210> 17
<211> 4
<212> PRT
<213> synthetic construct

<220>
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<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Cmp), i.e. N-alpha-cyclopropylmethyltyrosine

<220>

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<221> MOD_RES
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 17

Tyr Xaa Phe Phe
1

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<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Hex), i.e. N-alpha-hexyltyrosine

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<221> MOD_RES
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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Tyr Xaa Phe Phe
1

<210> 19
<211> 4
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<213> synthetic construct

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<221> MOD_RES
<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Et2), i.e. N-alpha-diethyltyrosine

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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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<212> PRT
<213> synthetic construct

<220>
<221> MOD_RES
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<222> (1)..(1)
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
<221> MOD_RES
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 20

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1

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<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<222> (4)..(4)
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<400> 21

Tyr Xaa Phe Phe
1

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<213> synthetic construct

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Tyr is H-Tyr(3-F), i.e. 3-fluorotyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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1

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<222> (1)..(1)
<223> Tyr is H-Tyr(3-Cl), i.e. 3-Chlorotyrosine

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<222> (2)..(2)
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Tyr Xaa Phe Phe
1

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<213> synthetic construct

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<222> (1)..(1)
<223> Tyr is H-Tyr(3-Br), i.e. 3-bromotyrosine

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<222> (2)..(2)
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<400> 24

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1

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<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin
n

<220>
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Tyr Xaa Phe Phe
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<222> (1)..(1)
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
<221> MOD_RES
<222> (2)..(3)
<223> nonpeptidyl bond

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin
n

<220>
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<223> AMIDATION

<400> 26

Tyr Xaa Phe Phe
1

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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin
n
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<220>
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<400> 27

Tyr Xaa Phe Phe
1

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<213> synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH₂-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 28

Tyr Xaa Phe Phe
1

<210> 29
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<220>
<221> MOD_RES
<222> (1)..(1)
<223> Tyr is Tyr(NMe), i.e. N-methyltyrosine

<220>
<221> MOD_RES
<222> (2)..(2)
<223> Xaa is Tic-psi-[CH₂-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

<220>
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<222> (3)..(3)
<223> Phe is -NH]Hfe, i.e. homophenylalanine

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1

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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<222> (3)..(3)
<223> Gly is Phg, i.e. phenylglycine

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Tyr Xaa Gly Phe
1

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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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Tyr Xaa Trp Phe
1

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<222> (4)..(4)
<223> AMIDATION

<400> 32

Tyr Xaa Trp Phe
1

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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Tyr Xaa His Phe
1

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<220>
<221> MOD_RES
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<223> Ala is 2-Nal, i.e. 3-(2'-naphthyl)alanine

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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<222> (3)..(3)
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Tyr Xaa Xaa Phe

1

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<220>
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<222> (4)..(4)
<223> Phe is Phe(pNO₂), i.e. 4-nitrophenylalanine

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Tyr Xaa Phe Phe
1

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<220>
<221> MOD_RES
<222> (4)..(4)
<223> Phe is Phe(pNO₂), i.e. 4-nitrophenylalanine

<400> 37

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1

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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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Tyr Xaa Phe Phe Val Val Gly
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Tyr Xaa Trp Phe Tyr Pro Ser
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<222> (4)..(4)
<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<220>
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<222> (7)..(7)
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<400> 42

Tyr Xaa Trp Phe Tyr Pro Ser
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<223> Nle

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<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION
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<211> 3

<212> PRT

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<220>

<221> MOD_RES

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

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<210> 45

<211> 3

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<213> synthetic construct

<220>

<221> MOD_RES

<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD_RES

<222> (3)..(3)

<223> AMIDATION

<400> 45

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<211> 3

<212> PRT

<213> synthetic construct

<220>

<221> MOD_RES

<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

n

<220>

<221> MOD_RES

<222> (2)..(3)

<223> nonpeptidyl bond

<400> 46

Tyr Xaa Phe
1

<210> 47
<211> 4
<212> PRT
<213> synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e. 3-methyl-1,2,3,4-tetrahydroisoquinolin

<220>
<221> MOD_RES
<222> (2)..(3)
<223> nonpeptidyl bond

<400> 47

Tyr Xaa Phe Phe
1

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<400> 48

Tyr Gly Gly Phe Met
1 5

<210> 49
<211> 6
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<213> synthetic construct

<400> 49

Tyr Gly Gly Phe Met Lys
1 5

<210> 50
<211> 6
<212> PRT
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<400> 50

Tyr Gly Gly Phe Leu Lys
1 5

<210> 51

<211> 6
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<220>
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<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<400> 51

Tyr Gly Gly Phe Leu Lys
1 5

*E1
OMC*
<210> 52
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<212> PRT
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<223> NH2 of Tyr is blocked by butyloxycarbonyl group

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<222> (6)..(6)
<223> polymer connected to epsilon-amino group

<400> 52

Tyr Gly Gly Phe Leu Lys
1 5